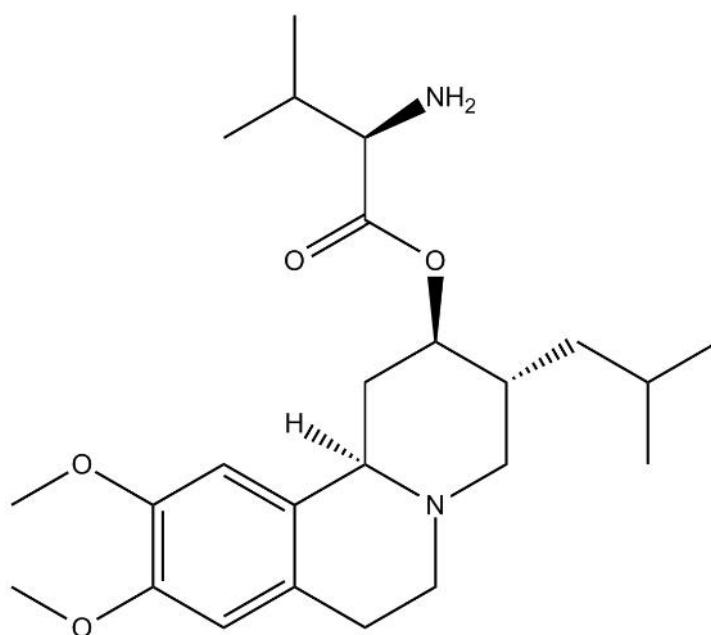


## Drug Profile

# Valbenazine

**Alternative Names:** INGREZZA; MT 5199; NBI-98854; Valbenazine-tosylate; VMAT2-inhibitor-Neurocrine-Biosciences

Latest Information Update: 09 Aug 2017



## At a glance

**Originator** Neurocrine Biosciences

**Developer** Mitsubishi Tanabe Pharma Corporation; Neurocrine Biosciences

**Class** 3-ring heterocyclic compounds; Amino acids; Neuropsychotherapeutics; Small molecules

**Mechanism of Action** Vesicular monoamine transporter 2 inhibitors

**Orphan Drug Status** No

**New Molecular Entity** Yes

## Highest Development Phases

**Marketed** Drug-induced dyskinesia

**Phase II** Gilles de la Tourette's syndrome

**Discontinued** Huntington's disease; Schizophrenia

## Most Recent Events

**03 Aug 2017** Neurocrine Biosciences files sNDA for valbenazine 80mg capsules for treatment of patients with Drug-induced dyskinesia in USA

**03 Aug 2017** US FDA assigns PDUFA action date of 14/10/2017 for valbenazine 80mg capsules for Drug-induced dyskinesia

**03 Aug 2017** Primary endpoint not met in the phase II T-Force GREEN trial in Gilles de la Tourette's syndrome

## Development Overview

### Introduction

Valbenazine, a highly selective, small-molecule vesicular monoamine transporter-2 (VMAT2) inhibitor is being developed by Neurocrine Biosciences for the treatment of a variety of central nervous system disorders, particularly involuntary hyperkinetic movement disorders such as drug-induced tardive dyskinesia and Tourette's syndrome. VMAT2 is a protein in the brain that packages neurotransmitters, such as dopamine, for transport and release in pre-synaptic neurons. The drug regulates levels of dopamine release during nerve communication, but has minimal impact on vesicular monoamine transporter-1 (VMAT1), other receptors including dopaminergic (D2), serotonergic, adrenergic, histaminergic, or muscarinic; transporters, ion channels or other monoamines, which may help to reduce the likelihood of "off-target" side effects. In addition, sustained plasma and brain concentrations of the active drug help to minimise the potential side effects associated with excessive dopamine depletion and allows for once daily dosing. Valbenazine has been launched for drug-induced dyskinesia in patients with schizophrenia or schizoaffective disorder in the US. Phase II development is also underway in the US for the treatment of adults and paediatric patients with Tourette's syndrome.

Valbenazine was also under phase I and preclinical development for chorea associated with Huntington's disease and Schizophrenia, respectively, however, the development in these indications appears to have been discontinued.

Neurocrine intends to maintain certain commercial rights to valbenazine, for evolution into a fully-integrated pharmaceutical company.

### Company Agreements

In March 2015, Neurocrine Biosciences entered into an exclusive collaboration and licensing agreement with Mitsubishi Tanabe Pharma Corporation for the development and commercialisation of valbenazine in Asia, including Japan, China, South Korea, Philippines, Indonesia, Taiwan, Singapore, Malaysia, Thailand, and Hong Kong. Under the terms of the agreement, Neurocrine is entitled to receive an initial payment of \$US 30 million and an additional milestone payments of up to \$US85 million based on the development and commercialisation of the product in Asia. The company is also eligible to receive royalties from Mitsubishi Tanabe based on the sales of the product in Asia. Neurocrine will provide support to Mitsubishi Tanabe for the clinical development of the product in patients with chorea associated with Huntington's disease and tardive dyskinesia. Mitsubishi Tanabe intends to focus initially on the development of valbenazine for the treatment of chorea associated with Huntington's disease and tardive dyskinesia. Neurocrine will retain commercialisation rights to the product in North America, Europe and other countries outside of Asia[1].

### Key Development Milestones

#### Tardive dyskinesia (Drug-induced dyskinesia)

In April 2017, the US FDA approved valbenazine capsules (INGREZZA™), for the treatment of tardive dyskinesia and subsequently launched the drug. The FDA had assigned a Prescription Drug User Fee Act (PDUFA) target action date of April 11, 2017[2][3][4][5]. In October 2016, the US FDA accepted for priority review, the New Drug Application (NDA) for valbenazine, for the treatment of tardive dyskinesia, which was submitted in August 2016. The application was based on results from the Kinect 2 and Kinect 3 clinical trials [see below], in addition to 18 clinical trials, extensive preclinical testing and drug manufacturing data[6][7]. The US FDA conditionally accepted the proprietary name INGREZZA™ in August 2016, for valbenazine[8].

In June 2017, Neurocrine Biosciences submitted a supplemental New Drug Application (sNDA) with

the US FDA for the approval of 80mg capsules of valbenazine for the treatment of tardive dyskinesia. Pending acceptance of the sNDA, the company has been advised that the PDUFA date is October 14, 2017[9].

The randomised, double-blind phase III Kinect 3 study met its primary efficacy endpoint of change-from-baseline in the Abnormal Involuntary Movement Scale (AIMS) at week six in the 80mg once-daily dosing group compared to placebo as assessed by expert central blinded video raters. In July 2016, Neurocrine Biosciences completed the phase III Kinect 3 study designed to assess the efficacy of valbenazine in patients with moderate to severe tardive dyskinesia with underlying mood disorder, schizophrenia or schizoaffective disorder (NBI-98854-1304; NCT02274558). The placebo-controlled trial was initiated in October 2014[10][11][12]. In August 2015, the randomised trial completed enrolment of 234 patients in the US, Canada and Puerto Rico, who received valbenazine at 40mg or 80mg, or placebo, once-daily for 6 weeks. This was followed by an extension consisting of active treatment through to 48 weeks. In the long-term extension phase, patients were eligible to continue for up to 42 weeks of additional valbenazine treatment. A total of 198 subjects entered the extension phase; 124 completed treatment and 121 completed follow-up. Positive results were presented at the 69th Annual Meeting of the American Academy of Neurology (AAN-2017)[13][14][15][16][17][18].

In March 2017, Neurocrine completed the one-year, phase III Kinect 4 trial that evaluated the safety and tolerability of valbenazine, administered once-daily, for the treatment of patients with tardive dyskinesia (NBI-98854-1402, NCT02405091). The open-label trial was initiated in March 2015, and enrolled 168 patients in the US, Canada and Puerto Rico. Data obtained from the Kinect 4 trial will be used to support the NDA filing[19][20][21][22].

In July 2017, Neurocrine Biosciences completed a phase IIIb roll-over study that provided an open label access to valbenazine until the patients completed 72 weeks of treatment or the drug is anticipated to be commercially available (NBI-98854-1506; NCT02736955)[9]. The study was initiated in March 2016 in the US; it enrolled 150 patients with tardive dyskinesia who completed the Kinect 3 or Kinect 4 studies[23].

In June 2017, Mitsubishi Tanabe Pharma initiated a phase II/III trial to evaluate the efficacy and safety of valbenazine for the treatment in patients with moderate to severe tardive dyskinesia (MT5199J02; J-KINECT, NCT03176771). Valbenazine will be administered once daily (capsule) for a maximum of 48 weeks. Evaluation of the severity of tardive dyskinesia symptoms is the defined primary endpoint of the trial. The double-blind, randomised, placebo-controlled, multicenter, parallel, fixed-dose trial intends to enrol approximately 240 patients in Japan. The placebo-controlled period is 6 weeks and the valbenazine extended administration period is 42 weeks[24][25]

Neurocrine Biosciences released results in January 2014 showing that the phase II Kinect 2 trial had met its primary endpoint. The results demonstrated significant improvements in the Abnormal Involuntary Movement Scale (AIMS) score at 6 weeks in patients treated with valbenazine at dosages of  $\leq 75$  mg/day, compared with those who received placebo. These results were in contrast to results from the earlier phase II Kinect trial, in which valbenazine lacked efficacy at those dose levels. Based on these outcomes and 12 week data from the Kinect study (including its extension-study), Neurocrine Biosciences held an End-of-Phase-II meeting with the US FDA in June 2014[26][27][28][29].

Neurocrine completed the 6-week, phase IIb Kinect 2 Study in December 2013, that assessed the efficacy of once-daily valbenazine in patients with moderate-to-severe, drug-induced tardive dyskinesia and an underlying mood disorder, schizophrenia or schizoaffective disorder, or a gastrointestinal disorder (NBI-98854-1202; NCT01733121)[30]. The randomised, double-blind, placebo-controlled, dose-titration trial completed enrolment of 102 patients in the US and Puerto Rico in October 2013. The intention-to-treat population included 89 patients. The trial was initiated in December 2012[10][31][28][29][32].

In September 2013, Neurocrine reported results from the phase II Kinect Study, which showed that the primary endpoint had not been met, but improvements were observed when valbenazine was administered at a dosage of 100 mg/day. Neurocrine initiated the randomised, double-blind, placebo-

controlled phase IIb Kinect trial in October 2012 (NBI-98854-1201; NCT01688037). The trial assessed the efficacy, safety and tolerability of valbenazine capsules for the treatment of drug-induced tardive dyskinesia in patients with schizophrenia or schizoaffective disorder. Patients received placebo, or valbenazine at a dosage of either 50 mg/day for 6 weeks, or 100 mg/day for 2 weeks then 50 mg/day for the following 4 weeks. The trial recruited 109 patients in the US and Puerto Rico[33][28][32][34][35][36]. The results showed a significant improvement in the Abnormal Involuntary Movement Scale (AIMS) score at 2 weeks in patients who initially received valbenazine 100 mg/day, compared with those who received placebo, but there was no significant improvement in the AIMS score at 6 weeks in either valbenazine group[11]. In January 2014, the company reported positive data from an extension study of the Kinetic study, whereby all patients were eligible to enter a six week open-label safety study of 50mg/day valbenazine followed by a four week washout period. The results suggested that valbenazine was well tolerated and improvements in the AIMS score were observed after 12 weeks of treatment in both treatment groups[27].

A phase II trial of valbenazine in patients with drug-induced tardive dyskinesia and schizophrenia or schizoaffective disorder did not meet its endpoint when all trial sites were included, but the endpoint was met when one trial site that Neurocrine reported showed discrepancies between the clinical score and video record was excluded (NBI-98854-1101; NCT01393600). The trial was completed in February 2012. Valbenazine was generally safe and well tolerated during the study. The double-blind, randomised trial was initiated in August 2011 and enrolled 37 patients in the US[35][37].

Neurocrine Biosciences completed an open-label phase IIa trial of valbenazine in Canada in April 2011 for the treatment of tardive dyskinesia in patients with schizophrenia or schizoaffective disorder (NBI-98854-1001; NCT01267188). Patients received three 4-day periods of valbenazine at increasing doses of 12.5mg, 25mg and 50mg, administered once daily. The trial enrolled 10 patients and its primary endpoint was the Abnormal Involuntary Movement Scale (AIMS)[38][39]. In March 2011, positive preliminary results were reported for the initial cohort of six patients. Based on this data, the company is initiating the IND application process with the US FDA. The trial was initiated in January 2011 and enrolled 10 patients in Canada[40].

Phase I trial is underway for the treatment of tardive dyskinesia in Japan (Mitsubishi Tanabe Pharma Corporation pipeline, February 2017)[1][41].

Additional *in vivo* toxicology studies are underway to support longer dosing regimens[42].

In June 2011, Neurocrine Biosciences held a pre-IND meeting with the US FDA's Division of Psychiatry Products. As a result of this meeting, the company submitted the final IND to the FDA in July 2011[42].

Valbenazine was granted Fast Track designation by the US FDA in January 2012, for the treatment of neuroleptic-induced tardive dyskinesia[43]. In October 2014, valbenazine was granted Breakthrough Therapy designation by the agency for tardive dyskinesia[44].

## **Tourette's syndrome**

Neurocrine Biosciences plans pivotal phase III programme for Tourette's syndrome. Clinical data obtained from phase II programme will support the initiation of phase III development[45].

Neurocrine Biosciences initiated a phase II trial in July 2016, to evaluate long-term safety and tolerability of valbenazine in patients with Tourette's syndrome (NBI-98854-1601; NCT02879578). The open label, fixed-dose study intends to enrol approximately 180 patients in the US, of which 90 will be children and adolescents and 90 adult patients, who completed T-Force Green or T-Forward trials [see below]. Valbenazine will be evaluated for once-daily fixed doses for safety by standard clinical laboratory tests, monthly physician examination and safety scale assessments[46][47].

In August 2017, Neurocrine Biosciences announced that the primary endpoint was not met in the phase II T-Force GREEN trial, initiated in February 2016, which evaluated the safety and efficacy of

valbenazine for the treatment of paediatric (children and adolescents) patients with Tourette syndrome (NBI-98854-1501; NCT02679079). Paediatric Tourette subjects received once-daily dosing of the drug or placebo during a six-week treatment period. The primary endpoint was to determine the change in baseline between placebo and active groups, as assessed by Yale Global Tic Severity Scale (YGTSS) until week 6. The three-arm trial enrolled 94 patients (children and adolescents) in the US[48][49][50]. Exposure-response analysis showed that the selected doses for the trial were below the therapeutic range for adequate tic reduction in the majority of paediatric subjects and provided insight into the level of dosing required for future studies[9][51].

In January 2017, Neurocrine Biosciences completed the phase II T-Forward trial, which evaluated the safety, tolerability and efficacy of valbenazine administered od (qd) for the treatment of adult patients with moderate to severe Tourette Syndrome (NBI-98854-1505; NCT02581865). The adult Tourette patients received once-daily dosing of valbenazine or placebo during the eight-week treatment period. The primary endpoint was to determine the change in baseline between placebo and active groups, as assessed by Yale Global Tic Severity Scale (YGTSS) until week 8. The randomised, placebo-controlled, double-blind, parallel trial was initiated in October 2015 and recruited 124 patients in the US. Top-line results reported in January 2017[52][48][53][54].

Neurocrine Biosciences completed a 2-week phase Ib trial in December 2015, which assessed the safety, tolerability, pharmacokinetics and pharmacodynamics of once-daily valbenazine in paediatric patients with Tourette's syndrome (T-Force; NBI-98854-1403; NCT02256475). The open-label, multiple ascending dose trial enrolled 18 children (6 to 11 years of age) and approximately 18 adolescents (12 to 18 years of age), in the US. Each age group was subdivided into three dosing cohorts of six patients each. An independent review of both safety and pharmacokinetic data was planned, following completion of dosing of the first adolescent cohort. The second adolescent cohort was designed to be dosed in parallel with the first cohort of children. Subsequent dose escalations for children and adolescents was based on the safety and pharmacokinetic data from the previous cohort in each age group. The Yale Global Tic Severity Scale, the Premonitory Urge for Tics Scale, as well as an overall Clinical Global Impression in Tourette syndrome Scale was used to weekly evaluate the patient's Tourette's symptoms. Positive data were released by the company in December 2015[55][17][56][57].

Neurocrine Biosciences conducted preclinical studies to investigate the efficacy of valbenazine in Tourette's syndrome. These studies were designed to support the advancement of the compound into clinical development in patients with Tourette's syndrome[28][58].

## **Huntington's disease**

Phase I development of valbenazine was underway in Japan for the treatment of Huntington's disease. However, the development in this indication appears to be discontinued (Mitsubishi Tanabe Pharma Corporation pipeline, February 2017)[59].

## **Schizophrenia**

Preclinical studies of valbenazine were ongoing for the treatment of schizophrenia, in the US. However, the development in this indication was discontinued (Neurocrine Biosciences pipeline, April 2017)

## **Healthy volunteers/patients with hepatic impairment**

: Neurocrine Biosciences completed a phase I trial, in August 2013, that assessed the effect of ketoconazole on the pharmacokinetics of valbenazine in healthy volunteers (NBI-98854-1302; NCT01910480). The trial was initiated in July 2013 and enrolled 24 volunteers in the US[60].

Neurocrine Biosciences has completed two phase I safety studies in healthy male volunteers[61][62]. No serious adverse events or significant laboratory or ECG findings were recorded[63][64]. According to company reports, the findings from these studies included dose proportionality, adequate AUC for drug exposure, low variability, and a half-life that supported once daily dosing.

Neurocrine Biosciences completed a phase I trial in December 2013 which assessed the safety, tolerability and pharmacokinetics of single doses of valbenazine capsules in patients with mild, moderate or severe hepatic impairment (NBI-98854-1303; NCT01916993). The trial was initiated in August 2013 and enrolled 24 patients in the US[65].

## **Financing information**

During the first quarter of 2015, Neurocrine completed a public offering of shares of its common stock resulting in net proceeds of approximately \$US270 million. The funds will be used to support Neurocrine's clinical programmes, including commercialisation of valbenazine for the treatment of tardive dyskinesia[20].

During the first quarter of 2014, Neurocrine completed a public offering of shares of its common stock resulting in net proceeds of approximately \$US 133 million. The funds will be used to support Neurocrine's clinical programmes, including development of valbenazine for the treatment of tardive dyskinesia and advancement its development for Tourette 's syndrome[26].

## **Patent Information**

In January 2013, Neurocrine Biosciences were awarded two patents regarding valbenazine. One patent, European Patent Number 2 081 929, covers chemical compositions, pharmaceutical compositions and uses of various compounds including valbenazine. The patent expires in November 2027. A separate patent, US patent No. 8 357 697, covers the method of treating hyperkinetic movement disorders using valbenazine and will expire in November 2027[66].

Neurocrine Biosciences was issued a composition of matter patent (No. 8 039 627) on valbenazine in the US in June 2011, with an initial patent term extending to May 2029[42][66].

## Drug Properties & Chemical Synopsis

**Route of administration** PO

**Formulation** Capsule, unspecified

**Class** 3-ring heterocyclic compounds, Amino acids, Neuropsychotherapeutics, Small molecules

**Mechanism of Action** Vesicular monoamine transporter 2 inhibitors

**WHO ATC code**

No7 (Other Nervous System Drugs)

**EPhMRA code**

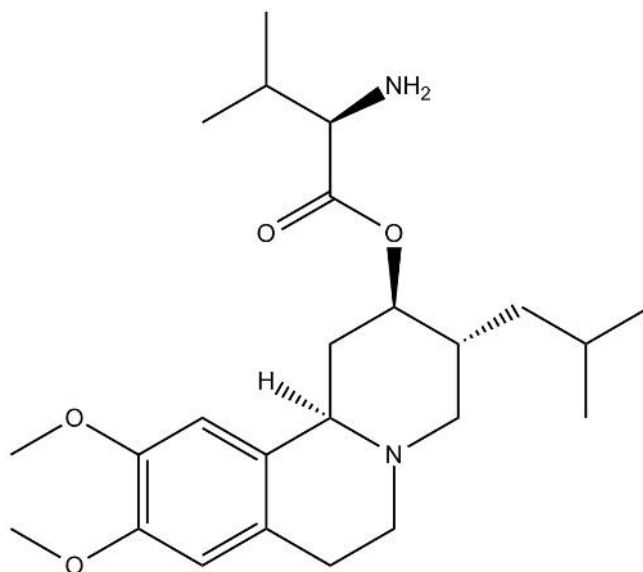
N7 (Other CNS Drugs)

**Chemical name** l-Valine, (2R,3R,11bR)-1,3,4,6,7,11b-hexahydro-9,10-dimethoxy-3-(2-methylpropyl)-2H-benzo[a]quinolizin-2-yl ester

**Molecular formula** C<sub>24</sub> H<sub>38</sub> N<sub>2</sub> O<sub>4</sub>

**SMILES** C(C(N)C(C)C)(=O)OC1C(CN2CCC3C(C2C1)=CC(=C(C=3)OC)OC)CC(C)C

**Chemical Structure**



**CAS Registry Number** 1025504-45-3

# Biomarkers Sourced From Trials

Indication	Biomarker Function	Biomarker Name	Number of Trials
drug-induced dyskinesia	Outcome Measure	Prolactin	<u><b>1</b></u>
drug-induced dyskinesia	Safety	Prolactin	<b>1</b>
schizoaffective disorder	Outcome Measure	Prolactin	<b>1</b>
schizoaffective disorder	Safety	Prolactin	<u><b>1</b></u>
schizophrenia	Outcome Measure	Prolactin	<b>1</b>
schizophrenia	Safety	Prolactin	<u><b>1</b></u>

# Biomarker

Drug Name	Biomarker Name	Biomarker Function
Valbenazine	<u>Prolactin</u>	Outcome Measure, Safety

For more detail, check out **BiomarkerBase:** the leading source of information about biomarkers used in drug development and diagnostic tests, tracking over 314010 biomarker uses worldwide by over 862 companies

# Trial Landscape

Indication	Phase 0	Phase I	Phase II	Phase III	Phase IV
Huntington's disease	-	<u>1</u>	-	-	-
Schizophrenia	-	<u>1</u>	<u>1</u>	-	-
Schizoaffective disorder	-	-	<u>1</u>	-	-
Gilles de la Tourette's syndrome	-	<u>2</u>	<u>4</u>	-	-
Drug-induced dyskinesia	-	<u>5</u>	<u>4</u>	<u>4</u>	<u>1</u>

# Development Status

## Summary Table

Indication	Patient Segment	Phase	Countries	Route / Formulation	Developers	Event Date
Drug-induced dyskinesia	-	Marketed	USA	PO / Capsule	Neurocrine Biosciences	21 Apr 2017
Drug-induced dyskinesia	-	Registered	Puerto Rico	PO / Capsule	Neurocrine Biosciences	11 Apr 2017
Drug-induced dyskinesia	-	Phase III	Canada	PO / Capsule	Neurocrine Biosciences	01 Oct 2014
Drug-induced dyskinesia	-	Phase II/III	Japan	PO / Capsule	Mitsubishi Tanabe Pharma Corporation	21 Jun 2017
Gilles de la Tourette's syndrome	-	Phase II	USA	PO / Capsule	Neurocrine Biosciences	01 Oct 2015
Gilles de la Tourette's syndrome	In adolescents, In children	Phase II	USA	PO / Capsule	Neurocrine Biosciences	02 Feb 2016
Huntington's disease	-	Discontinued (I)	Japan	PO / Capsule	Mitsubishi Tanabe Pharma Corporation	17 Apr 2017
Schizophrenia	-	Discontinued (Preclinical)	USA	PO / unspecified	Neurocrine Biosciences	20 Apr 2017

## Commercial Information

### Involved Organisations

Organisation	Involvement	Countries
Neurocrine Biosciences	Originator	USA
Neurocrine Biosciences	Owner	USA
Mitsubishi Tanabe Pharma Corporation	Licensee	China, Hong Kong, Indonesia, Japan, Malaysia, Philippines, Singapore, South Korea, Taiwan, Thailand

### Brand Names

Brand Name	Organisations	Indications	Countries
INGREZZA	Neurocrine Biosciences	Drug-induced dyskinesia	USA

## Scientific Summary

**Adverse Events Occasional:** Fatigue; Headache; Somnolence

### Adverse Events

#### Phase III

In the phase III Kinect 3 trial, valbenazine at the dose of 80 mg/day was well tolerated during the placebo-controlled treatment period. The frequency of adverse events was similar among all treatment groups. The randomized, double-blind, placebo-controlled trial enrolled 240 patients with moderate to severe tardive dyskinesia with underlying mood disorder, schizophrenia or schizoaffective disorder[16]. Additional safety results from the Kinect 3 study demonstrate that the most common AEs observed were somnolence (occurring at 5% or greater and twice placebo) and drooling. The frequency of treatment emergent adverse events were consistent with prior studies. No drug-drug interactions were identified in subjects who were administered a wide range of psychotropic and other concomitant medications[68][12].

#### Phase II

Valbenazine was generally well tolerated in patients with tardive dyskinesia in the phase II Kinect 2 trial. Treatment-emergent adverse events occurred in 43% of valbenazine recipients and 33% of placebo recipients. No drug-related serious adverse events were reported, and there were no study withdrawals due to treatment-related adverse events. Adverse events reported more frequently in the valbenazine group than the placebo group included fatigue (9.8% vs 4.1%) and headache (7.8% vs 4.1%). A total of 102 patients were included in the randomised Kinect 2 trial[10].

Mild transient somnolence occurred in 5.7% of patients who received valbenazine 50 mg/day for 6 weeks, or 100 mg/day for the first 2 weeks then 50 mg/day, in the phase II Kinect trial. The frequency of other adverse events was lower in the valbenazine groups than the placebo group. The randomised, double-blind, placebo-controlled Kinect trial included 109 patients[11]. During a six week open-label safety extension of the Kinect study, valbenazine was generally safe and well tolerated. The frequency of treatment-emergent adverse events, over 12 weeks, was 40% and similar to previous studies. The most common adverse event during the 12 week period was urinary tract infections in 6 patients but these were determined to be unrelated to the study. No drug-drug interactions were identified in patients receiving psychotropic or other concomitant medications. Patients from both treatment groups (42 who originally received placebo and 39 who received valbenazine) were eligible to receive valbenazine 50mg/day for a further six weeks during the open-label study[27].

Valbenazine was generally safe and well tolerated in a phase II trial in 37 patients with neuroleptic-induced tardive dyskinesia and schizophrenia or schizoaffective disorder. Patients received placebo or valbenazine 12.5 or 50 mg once-daily over a 2-week period. The frequency of treatment-emergent adverse events was 17% during the placebo period and 24% and 32% in the 12.5 mg and 50 mg treatment periods, respectively. There were no serious adverse events and the most common adverse event was headache. One patient in the 50 mg group discontinued due to akathisia. The Brief Psychiatric Rating Scale indicated the underlying psychiatric state of patients during the trial was stable or improving. No drug interactions were reported during the study[35].

Valbenazine was also well tolerated in a phase I study in healthy volunteers. There were no serious adverse events or clinically significant abnormalities or ECG findings observed[63].

#### Phase I:

Valbenazine was safe and well tolerated in the phase Ib T-force trial. The open-label, multiple ascending dose trial enrolled approximately 36 paediatric patients with Tourette's syndrome[55].

## Pooled Analysis

A pooled analysis of the KINECT, KINECT 3 and KINECT 4 studies demonstrated that valbenazine was well tolerated in adults with tardive dyskinesia who received valbenazine (ranging from 40 mg/day to 80 mg/day in the three studies) for 48 weeks. The most commonly observed treatment emergent adverse events (TEAEs) were somnolence (4.7%), fatigue (3.7%), and dry mouth (2.3%). Serious TEAEs were reported in 12.6% of the subjects. Dose reduction due to TEAEs was observed in 6.1% subjects, while 13.6% of subjects discontinued treatment due to TEAEs. Changes in vital signs, ECGs, and laboratory parameters (including hepatic function) were not clinically significant. No worsening of psychiatric symptoms or clinically significant drug-induced extrapyramidal symptoms were observed[67].

## Therapeutic Trials

### Phase II

In the phase II T-Forward trial, valbenazine od was associated with a significant improvement in overall symptoms of Tourette syndrome as evidenced by the Clinical Global Impression of Change ( $p=0.015$ ) in patients with moderate to severe Tourette Syndrome. The pre-specified primary endpoint, the change-from-baseline in the Yale Global Tic Severity Scale (YGTSS) at week 8 was not met ( $p=0.18$ ). The trial enrolled 124 patients[52][54].

### Phase I:

In the phase Ib T-Force trial, valbenazine demonstrated a mean reduction of 31% in Tourette syndrome symptoms from baseline scores in more than half of the clinical responders. The open-label, multiple ascending dose trial enrolled approximately 36 paediatric patients with Tourette's syndrome[55].

### Phase III

In the phase III Kinect 3 trial, treatment with 80 mg/day valbenazine resulted in significantly greater improvements from baseline in the Abnormal Involuntary Movement Scale (AIMS) score at week 6, compared with placebo. At week 6, the AIMS ratings reduced 3.2 points (Least-Squares Mean) for the 80mg once-daily group as compared to 0.1 in the placebo group ( $p<0.0001$ ). The randomized, double-blind, placebo-controlled trial enrolled 240 patients with with moderate to severe tardive dyskinesia (TD) with underlying mood disorder, schizophrenia or schizoaffective disorder[3][16]. Additional results from the phase III Kinect study demonstrate that the percentage of participants who achieved an AIMS response was higher in the valbenazine 80 mg/day group compared with placebo at all study visits. At the six-week timepoint, 40% ( $p<0.001$ ) of participants receiving 80 mg/day of valbenazine had at least a 50% improvement in AIMS dyskinesia as against only 8.7% patients who received placebo[68]. In an extension of the Kinect 3 trial, treatment with valbenazine demonstrated improvement in TD with mean score changes in both dose groups [80mg/day ( $n=63$ ), -4.8; 40mg/day ( $n=61$ ), -3.0] at week 48; AIMS score were 52% and 28%, respectively. However, AIMS scores increased from week 48 to week 52 (80mg/day, 6.2 to 9.8; 40mg/day, 6.8 to 8.4), indicating worsening of TD during the 4-week no-treatment period. Also, 76% and 59% of subjects showed clinically meaningful global improvements in mean week 48 Clinical Global Impression of Change (CGI-TD) scores. A total of 198 subjects entered the extension phase; 124 completed treatment and 121 completed follow-up[13][12].

### Phase II:

Treatment with valbenazine at dosages of up to up to 75 mg/day resulted in a significantly greater improvement from baseline in the Abnormal Involuntary Movement Scale (AIMS) score at week 6, compared with placebo, in the phase II Kinect 2 trial. Specifically, the AIMS score improved by 2.6 points in the valbenazine group versus 0.2 points in the placebo group ( $p = 0.0005$ ), as assessed by blinded central review, meeting the primary endpoint of the trial. The randomised, double-blind trial

included 89 patients in the intention-to-treat population. Additional results showed that the AIMS responder rate was better in the valbenazine group than the placebo group (49% vs 18%, respectively;  $p = 0.002$ ), and Clinical Global Impressions of Change-Tardive Dyskinesia scores and responder rates were also better in the active group (67% vs. 16%,  $p < 0.0001$ )[69][10].

A phase II trial of valbenazine did not meet its endpoint when all trial sites were included, but the endpoint was met when one trial site that Neurocrine reported showed discrepancies between the clinical score and video record was excluded. Patients received placebo or valbenazine 12.5 mg or 50 mg once-daily over a 2-week period. When all clinical trial sites were included in the analysis, there was no significant change in the AIMS score from baseline, the primary endpoint, in the treatment groups compared with the control group. In addition, the investigator-reported Global Impression - Tardive Dyskinesia score was 52%, 65% and 60% in the placebo and valbenazine 12.5 mg and 50 mg groups, respectively. The Patient Global Impression of Change was 39% in the placebo group compared with 53% and 60% in the valbenazine 12.5 mg and 50 mg groups respectively. When the trial site that the company reported showed discrepancies between the clinical score and video record was excluded, the Abnormal Involuntary Movement Scale showed a significant improvement in the valbenazine 50 mg treatment group compared with placebo. The 50 mg cohort showed a significant reduction in tardive dyskinesia symptoms at the end of 2 weeks active treatment by an average of 9.2 points. This post-hoc analysis also showed treatment with valbenazine was associated with improvement in the Clinical Global Impression - Tardive Dyskinesia (46%, 67% and 80% in placebo, valbenazine 12.5 and 50 mg groups, respectively) and the Patient Global Impression of Change (38%, 62% and 80% in the placebo, valbenazine 12.5 and 50 mg groups, respectively). This trial enrolled 37 patients with neuroleptic-induced tardive dyskinesia and schizophrenia or schizoaffective disorder[35].

In contrast to the Kinect 2 trial, the primary endpoint was not met in the phase II Kinect trial. The primary endpoint of the randomised, double-blind trial was the change from baseline in the Abnormal Involuntary Movement Scale (AIMS) score at 6 weeks. At this time-point, there was no significant difference between the valbenazine and placebo groups, in either the intention-to-treat or per-protocol populations. In this trial, patients received placebo, or valbenazine at a dosage of either 50 mg/day for 6 weeks, or 100 mg/day for 2 weeks then 50 mg/day for the following 4 weeks. A total of 109 patients were enrolled. Despite not meeting the primary endpoint, the data showed a significant improvement in the change from baseline in the AIMS score at 2 weeks in patients who received valbenazine 100 mg/day, compared with those who received placebo. The AIMS responder rate was also better in recipients of valbenazine 100 mg/day than placebo recipients at the 2-week analysis[11]. However by week 12, during an open-label extension period in which patients from both treatment groups were treated with 50mg/day valbenazine for a further six weeks, there was a marked reduction from baseline in AIMS scores for both groups with a 54% responder rate ( $\geq 50\%$  reduction in AIMS from baseline). Treating clinicians noted that approximately 61% of patients receiving valbenazine were 'much improved' or 'very much improved' at week 12, as determined by the Clinical-Global-Impression-Tardive Dyskinesia (CGI-TD) evaluation. At the end of a four week washout period, these CGI-TD outcomes were seen in 29% of the patients[27].

Treatment with valbenazine reduced the symptoms of tardive dyskinesia in an open-label phase IIa trial (NCT01267188) in six patients with schizophrenia. Results of the trial showed that 12 days of treatment with valbenazine at increasing doses of 12.5mg, 25mg and 50mg, administered once daily, reduced the mean AIMS score from 14.3 to 8.4, a reduction of 41.3%[40].

# Future Events

Expected Date	Event Type	Description	Updated
31 Dec 2017	Trial Update	Neurocrine Biosciences plans a phase IIb trial for Gilles de la Tourette's syndrome in late 2017 [9]	09 Aug 2017
14 Oct 2017	Regulatory Status	US FDA assigns PDUFA action date of 14/10/2017 for valbenazine 80mg capsules for Drug-induced dyskinesia [9]	09 Aug 2017
30 Jun 2017	Trial Update	Mitsubishi Tanabe Pharma Corporation plans a phase II/III trial for Drug-induced dyskinesia in Japan (NCT03176771)	20 Jul 2017

## Development History

Event Date	Update Type	Comment
03 Aug 2017	Regulatory Status	Neurocrine Biosciences files sNDA for valbenazine 80mg capsules for treatment of patients with Drug-induced dyskinesia in USA <sup>[9]</sup> Updated 09 Aug 2017
03 Aug 2017	Regulatory Status	US FDA assigns PDUFA action date of 14/10/2017 for valbenazine 80mg capsules for Drug-induced dyskinesia <sup>[9]</sup> Updated 09 Aug 2017
03 Aug 2017	Scientific Update	Primary endpoint not met in the phase II T-Force GREEN trial in Gilles de la Tourette's syndrome <sup>[9]</sup> Updated 09 Aug 2017
03 Aug 2017	Trial Update	Neurocrine Biosciences completes a phase IIIb roll-over trial in Drug-induced dyskinesia in USA (NCT02736955) <sup>[9]</sup> Updated 09 Aug 2017
03 Aug 2017	Trial Update	Neurocrine Biosciences plans a phase IIb trial for Gilles de la Tourette's syndrome in late 2017 <sup>[9]</sup> Updated 09 Aug 2017
21 Jun 2017	Phase Change - II/III	Phase-II/III clinical trials in Drug-induced dyskinesia in Japan (PO) (NCT03176771) Updated 20 Jul 2017
07 Jun 2017	Trial Update	Mitsubishi Tanabe Pharma Corporation plans a phase II/III trial for Drug-induced dyskinesia in Japan (NCT03176771) Updated 20 Jul 2017
10 May 2017	Trial Update	Neurocrine Biosciences plans pivotal phase III trials for Gilles de la Tourette's syndrome <sup>[45]</sup> Updated 19 May 2017
22 Apr 2017	Scientific Update	Efficacy data from the phase III KINECT 3 extension trial in Drug-induced dyskinesia presented at the 69th Annual Meeting of the American Academy of Neurology (AAN-2017) <sup>[13]</sup> Updated 02 Jul 2017
22 Apr 2017	Scientific Update	Adverse events data from a pooled analysis of phase II and III KINECT, KINECT 3 and KINECT 4 trials in Drug-induced dyskinesia presented at the 69 <sup>th</sup> Annual Meeting of the American Academy of Neurology (AAN-2017) <sup>[67]</sup> Updated 14 Jun 2017
21 Apr 2017	Phase Change - Marketed	Launched for Drug-induced dyskinesia in USA (PO) <sup>[2]</sup> Updated 27 Apr 2017
20 Apr 2017	Phase Change - Discontinued(Preclinical)	Discontinued - Preclinical for Schizophrenia in USA (PO) Updated 20 Apr 2017
17 Apr 2017	Phase Change - Discontinued(I)	Discontinued - Phase-I for Huntington's disease in Japan (PO) Updated 17 Apr 2017
11 Apr 2017	Phase Change - Registered	Registered for Drug-induced dyskinesia in USA and Puerto Rico (PO) - First global approval <sup>[3]</sup> Updated 12 Apr 2017

21 Mar 2017	Scientific Update	Updated adverse events and efficacy data from the phase III Kinect 3 study in Tardive dyskinesia released by Neurocrine Biosciences [68] Updated 24 Mar 2017
01 Mar 2017	Trial Update	Neurocrine Biosciences completes the phase-III Kinect 4 trial in Drug-induced dyskinesia in USA, Canada and Puerto Rico (NCT02405091) Updated 29 Mar 2017
17 Jan 2017	Scientific Update	Top-line efficacy results from a phase II trial in Gilles de la Tourette's syndrome reported by Neurocrine Biosciences [52] Updated 31 Jan 2017
17 Jan 2017	Trial Update	Neurocrine Biosciences completes the T-FORWARD phase II trial for Gilles de la Tourette's Syndrome in USA (PO) [52] Updated 31 Jan 2017
05 Jan 2017	Regulatory Status	US FDA cancelled the Psychopharmacologic Drugs Advisory Committee meeting which was previously scheduled to happen in February 2017 [4] Updated 09 Jan 2017
15 Dec 2016	Biomarker Update	Biomarkers information updated Updated 10 Jun 2017
11 Oct 2016	Regulatory Status	FDA assigns PDUFA action date of 11/04/2017 for valbenazine for Drug-induced dyskinesia [6] Updated 12 Oct 2016
11 Oct 2016	Regulatory Status	Valbenazine receives priority review status for Drug-induced dyskinesia in USA [6] Updated 12 Oct 2016
29 Aug 2016	Phase Change - Preregistration	Preregistration for Drug-induced dyskinesia in USA and Puerto Rico (PO) [7] Updated 31 Aug 2016
28 Jul 2016	Trial Update	Neurocrine Bioscience initiates enrolment in a phase II trial for Gilles de la Tourette's syndrome (Treatment-experienced, In children, In adolescents, In adults) in USA (PO) [46] Updated 02 Aug 2016
16 Jul 2016	Phase Change - No development reported	No recent reports of development identified for preclinical development in Schizophrenia in USA (PO) Updated 16 Jul 2016
01 Jul 2016	Trial Update	Neurocrine Biosciences completes the phase-III KINECT 3 trial in Drug-induced dyskinesia in USA, Canada and Puerto Rico (NCT02274558) Updated 30 Aug 2016
11 May 2016	Phase Change - I	Phase-I clinical trials in Drug-induced dyskinesia in Japan (PO) Updated 29 Jul 2016
11 May 2016	Phase Change - I	Phase-I clinical trials in Huntington's disease in Japan (PO) Updated 29 Jul 2016
01 Mar 2016	Trial Update	Neurocrine Biosciences initiates a phase IIIb roll-over study for Drug-induced dyskinesia in USA (NCT02736955) Updated 21 Apr 2016
02 Feb 2016	Phase Change - II	Phase-II clinical trials in Gilles de la Tourette's syndrome (In adolescents, In children) in USA (PO) Updated 03 Feb 2016

16 Dec 2015	Scientific Update	Adverse events and efficacy data from the phase Ib T-Force trial in Gilles de la Tourette's Syndrome (In children, In adolescents) released by Neurocrine Biosciences <sup>[55]</sup> Updated 19 Dec 2015
16 Dec 2015	Trial Update	Neurocrine Biosciences plans a phase II trial for Gilles de la Tourette's Syndrome (In children, In adolescents) in USA (PO) <sup>[55]</sup> Updated 19 Dec 2015
16 Dec 2015	Trial Update	Neurocrine Biosciences completes the phase Ib T-Force trial for Gilles de la Tourette's Syndrome (In children, In adolescents) in USA (PO) <sup>[55]</sup> , NCT02256475) Updated 19 Dec 2015
13 Oct 2015	Scientific Update	Safety and efficacy results from the phase III Kinect 3 trial in drug-induced dyskinesia released by Neurocrine Biosciences <sup>[16]</sup> Updated 13 Oct 2015
01 Oct 2015	Phase Change - II	Phase-II clinical trials in Gilles de la Tourette's syndrome in USA (PO) Updated 08 Nov 2015
13 Aug 2015	Trial Update	Neurocrine Biosciences completes enrolment in a phase III Kinect 3 trial in drug-induced dyskinesia in USA, Canada and Puerto Rico <sup>[17]</sup> Updated 17 Aug 2015
31 Mar 2015	Licensing Status	Neurocrine Biosciences and Mitsubishi Tanabe Pharma Corporation enter into an exclusive agreement for the development and commercialisation of valbenazine in Japan, China, South Korea, Philippines, Indonesia, Taiwan, Singapore, Malaysia, Thailand, and Hong Kong <sup>[1]</sup> Updated 03 Apr 2015
01 Mar 2015	Trial Update	Neurocrine Biosciences initiates a phase-III clinical trial in Drug-induced dyskinesia in Puerto Rico (PO) (NCT02405091) Updated 08 Jun 2015
30 Oct 2014	Regulatory Status	Valbenazine receives breakthrough therapy designation for Tardive dyskinesia in USA <sup>[44]</sup> Updated 02 Nov 2014
20 Oct 2014	Phase Change - III	Phase-III clinical trials in Drug-induced dyskinesia in USA (PO) (NCT02405091) Updated 22 Oct 2014
20 Oct 2014	Trial Update	Neurocrine Biosciences initiates a phase III Kinect 3 trial in drug-induced dyskinesia in USA <sup>[18]</sup> Updated 22 Oct 2014
01 Oct 2014	Phase Change - III	Phase-III clinical trials in Drug-induced dyskinesia in Canada and Puerto Rico after October 2014 (PO) (NCT02274558) Updated 17 Aug 2015
01 Sep 2014	Phase Change - I	Phase-I clinical trials in Gilles de la Tourette's syndrome (In children, In adolescents) in USA (PO) Updated 06 Oct 2014
06 Aug 2014	Regulatory Status	Neurocrine Biosciences announces intention to submit NDA for Drug-induced dyskinesia to US FDA in 2016 <sup>[15]</sup> Updated 13 Oct 2014

31 Mar 2014	Regulatory Status	Neurocrine submits a request for an End-of-Phase II meeting for Tardive dyskinesia to the US FDA <sup>[26]</sup> Updated 09 May 2014
09 Jan 2014	Scientific Update	Final adverse events and efficacy data from an open-label extension of the phase IIb KINECT trial in Drug-induced dyskinesia released by Neurocrine Biosciences <sup>[27]</sup> Updated 21 Jan 2014
06 Jan 2014	Scientific Update	Final efficacy and adverse data from the phase II Kinect 2 trial in Drug-induced dyskinesia released by Neurocrine Biosciences <sup>[10]</sup> Updated 08 Jan 2014
31 Dec 2013	Trial Update	Neurocrine Biosciences completes a phase I trial for Drug-induced dyskinesias (in patients with hepatic impairment) in the USA (NCT01916993) Updated 24 Feb 2014
01 Dec 2013	Trial Update	Neurocrine Biosciences completes the phase IIb Kinect 2 Study for Tardive dyskinesia in USA (NCT01733121) Updated 13 Jan 2014
25 Oct 2013	Trial Update	Neurocrine Biosciences completes enrolment in the phase IIb Kinect 2 trial for Drug-induced dyskinesias in USA & Puerto Rico (NCT01733121) Updated 12 Nov 2013
12 Sep 2013	Trial Update	Neurocrine Biosciences initiates enrolment in a phase I trial for Drug-induced dyskinesias (patients with hepatic impairment) in USA (NCT01916993) Updated 12 Sep 2013
10 Sep 2013	Scientific Update	Final efficacy and adverse events data from the phase II Kinect trial in Drug-induced dyskinesia released by Neurocrine Biosciences <sup>[11]</sup> Updated 12 Sep 2013
31 Aug 2013	Trial Update	Neurocrine Biosciences completes a phase I pharmacokinetics trial in Healthy volunteers in the US (NCT01910480) Updated 12 Sep 2013
02 Aug 2013	Trial Update	Neurocrine Biosciences plans a phase I trial in patients with hepatic impairment in USA (NCT01916993) Updated 16 Aug 2013
01 Jul 2013	Trial Update	Neurocrine Biosciences initiates enrolment in a phase I pharmacokinetics trial in Healthy volunteers in the US (NCT01910480) Updated 08 Aug 2013
01 Jul 2013	Trial Update	Neurocrine Biosciences completes enrolment in the phase IIb KINECT trial for Drug-induced dyskinesia in USA & Puerto Rico (NCT01688037) Updated 02 Jul 2013
03 May 2013	Phase Change - II	Phase-II clinical trials in Drug-induced dyskinesia in Puerto Rico (PO) Updated 02 Jul 2013
23 Jan 2013	Patent Information	Neurocrine Biosciences has patent protection for valbenazine in USA and European Union <sup>[66]</sup> Updated 17 Apr 2017

31 Dec 2012	Phase Change - Preclinical	Preclinical trials in Gilles de la Tourette's syndrome in USA (PO) Updated 12 Feb 2013
18 Dec 2012	Trial Update	Neurocrine Biosciences initiates enrolment in the phase IIb Kinect 2 Study for Tardive dyskinesia in USA (NCT01733121) Updated 20 Dec 2012
01 Oct 2012	Trial Update	Neurocrine Biosciences initiates enrolment in a phase IIb trial for Drug-induced dyskinesia in USA (NCT01688037) Updated 02 Oct 2012
01 Oct 2012	Trial Update	Neurocrine Biosciences plans a phase IIb trial for Drug-induced dyskinesia <sup>[32]</sup> Updated 02 Oct 2012
26 Mar 2012	Scientific Update	Final efficacy and adverse events data from a phase II trial in Drug-induced dyskinesia in patients with schizophrenia or schizoaffective disorder released by Neurocrine <sup>[35]</sup> Updated 27 Mar 2012
29 Feb 2012	Trial Update	Neurocrine Biosciences completes a Phase-II trial in Drug-induced dyskinesia in patients with schizophrenia or schizoaffective disorder in USA (NCT01393600) Updated 16 Mar 2012
25 Jan 2012	Regulatory Status	NBI 98854 receives Fast Track designation for Drug-induced dyskinesia [PO,Capsule] in USA Updated 26 Jan 2012
06 Jan 2012	Trial Update	Neurocrine Biosciences completes enrolment in its phase II trial for Drug-induced dyskinesia in USA (NCT01393600) Updated 18 Jan 2012
24 Aug 2011	Phase Change - II	Phase-II clinical trials in Drug-induced dyskinesia in USA (PO) Updated 08 Sep 2011
23 Jun 2011	Patent Information	Neurocrine Biosciences receives patent allowance for Valbenazine in USA <sup>[42]</sup> Updated 17 Apr 2017
18 Apr 2011	Trial Update	Neurocrine Biosciences completes a phase II trial in Drug-induced dyskinesia in Canada (NCT01267188) Updated 05 May 2011
05 Apr 2011	Scientific Update	Efficacy data from a phase IIa trial in Drug-induced dyskinesia released by Neurocrine Biosciences <sup>[40]</sup> Updated 07 Apr 2011
27 Jan 2011	Phase Change - II	Phase-II clinical trials in Drug-induced dyskinesia in Canada (PO) Updated 15 Feb 2011
31 Dec 2010	Phase Change - Preclinical	Preclinical trials in Schizophrenia in USA (unspecified route) Updated 23 Feb 2011
18 Oct 2010	Trial Update	Neurocrine Biosciences completes a second phase I trial in healthy volunteers in Canada Updated 20 Oct 2010
22 Dec 2009	Scientific Update	Interim adverse events data from a phase I trial released by Neurocrine Biosciences <sup>[63]</sup> Updated 23 Dec 2009

17 Nov 2009

Phase Change - I

Phase-I clinical trials in CNS disorders in  
Canada (unspecified route)  
Updated 17 Nov 2009

## References

1. Neurocrine Biosciences and Mitsubishi Tanabe Pharma Announce Agreement to Develop and Commercialize VMAT2 Inhibitor NBI-98854 for Movement Disorders in Japan and Other Select Asian Markets.  
**Media Release**
2. Neurocrine Announces INGREZZA(T) Long-Term Safety and Efficacy Data to be Presented at the 2017 American Academy of Neurology Annual Meeting.  
**Media Release**
3. Neurocrine Announces FDA Approval of INGREZZA(T) (valbenazine) Capsules as the First and Only Approved Treatment for Adults with Tardive Dyskinesia (TD) (with multimedia).  
**Media Release**
4. Neurocrine Provides Update on FDA Advisory Committee for INGREZZA(T) (valbenazine) for the Treatment of Tardive Dyskinesia.  
**Media Release**
5. Neurocrine Announces FDA Advisory Committee Meeting to Review INGREZZA(Tm) (valbenazine) New Drug Application for the Treatment of Tardive Dyskinesia.  
**Media Release**
6. Neurocrine Announces INGREZZA(TM) (valbenazine) New Drug Application for the Treatment of Tardive Dyskinesia has been Accepted for Priority Review by U.S. FDA.  
**Media Release**
7. Neurocrine Submits New Drug Application for Valbenazine for Treatment of Tardive Dyskinesia.  
**Media Release**
8. Neurocrine Announces FDA Conditional Acceptance of Proprietary Name INGREZZA(TM) for VMAT2 Inhibitor Valbenazine.  
**Media Release**
9. Neurocrine Biosciences Reports Second Quarter 2017 Results.  
**Media Release**
10. Neurocrine Announces Positive Results of VMAT2 Inhibitor NBI-98854 in Kinect 2 Study.  
**Media Release**
11. Neurocrine Announces Phase IIb Results Of VMAT2 Inhibitor NBI-98854 For Treatment Of Tardive Dyskinesia.  
**Media Release**
12. A Phase 3, Randomized, Double-Blind, Placebo-Controlled, Parallel, Fixed-Dose Study to Assess the Efficacy, Safety, and Tolerability of NBI-98854 for the Treatment of Tardive Dyskinesia  
**ctiprofile**
13. Factor S, Comella C, Correll C, Liang G, Burke J, O'Brien C. Efficacy of Valbenazine (NBI-98854) in Subjects with Tardive Dyskinesia: Results of a Long-Term Study (KINECT 3 Extension). AAN-2017 2017; abstr. 2643.  
Available from: URL: **<http://submissions.mirasmart.com/AAN2017/itinerary/login.asp>**
14. Neurocrine Biosciences Reports Second Quarter 2016 Results.  
**Media Release**
15. Neurocrine Biosciences Reports Second Quarter 2014 Results.  
**Media Release**
16. Neurocrine Announces Positive Results from Phase III Kinect 3 Study of NBI-98854 in Tardive Dyskinesia.  
**Media Release**
17. Neurocrine Announces Completion of Enrollment into Kinect 3 Tardive Dyskinesia Study.

**Media Release**

18. Neurocrine Announces Initiation Of Phase III Study For VMAT2 Inhibitor NBI-98854.

**Media Release**

19. Neurocrine Biosciences Reports First Quarter 2016 Results.

**Media Release**

20. Neurocrine Biosciences Reports First Quarter 2015 Results.

**Media Release**

21. Neurocrine Biosciences Reports Year-End 2014 Results and Provides Investor Update for 2015.

**Media Release**

22. A Phase 3, Open-Label, Safety and Tolerability Study of NBI-98854 for the Treatment of Tardive Dyskinesia

**ctiprofile**

23. Rollover Study for Continuing Valbenazine (NBI-98854) Administration for the Treatment of Tardive Dyskinesia

**ctiprofile**

24. Notice regarding the initiation of a phase 2/3 clinical trial in Japan for tardive dyskinesia patients for VMAT2 inhibitor MT-5199.

**Media Release**

25. A Phase 1b/2 trial of PCM-075 assessing safety in Acute-myeloid-leukaemia patients.

**ctiprofile**

26. Neurocrine Biosciences Reports First Quarter 2014 Results.

**Media Release**

27. Neurocrine Announces 12-Week Safety Results From Initial Phase IIB Study Of VMAT2 Inhibitor NBI-98854.

**Media Release**

28. Neurocrine Biosciences Reports First Quarter 2013 Results.

**Media Release**

29. Neurocrine Announces Start Of Second Phase IIB Study Of VMAT2 Inhibitor NBI-98854 For Treatment Of Tardive Dyskinesia.

**Media Release**

30. A Phase 2, Randomized, Double-Blind, Placebo-Controlled, Dose-Titration Study to Assess the Safety, Tolerability, and Efficacy of NBI-98854 for the Treatment of Tardive Dyskinesia

**ctiprofile**

31. Neurocrine Biosciences Reports Third Quarter 2013 Results.

**Media Release**

32. Neurocrine Announces Start Of Phase IIB Study Of VMAT2 Inhibitor NBI-98854 For Treatment Of Tardive Dyskinesia

**Media Release**

33. Neurocrine Announces Completion Of Enrollment Into Kinect Study For Treatment Of Tardive Dyskinesia.

**Media Release**

34. Neurocrine Biosciences Reports Second Quarter 2012 Results.

**Media Release**

35. Neurocrine Announces Phase II Results of VMAT2 Inhibitor NBI-98854 for Treatment of Tardive Dyskinesia.

**Media Release**

36. A Phase 2, Randomized, Double-Blind, Placebo-Controlled Study to Assess the Efficacy and Safety of NBI-98854 for the Treatment of Tardive Dyskinesia in Subjects With Schizophrenia or Schizoaffective Disorder

**ctiprofile**

37. A Phase 2, Double-Blind, Randomized, Placebo-Controlled, Two-Period Cross-Over Study to Evaluate the Efficacy and Safety of NBI-98854 for the Treatment of Tardive Dyskinesia in Subjects With Schizophrenia or Schizoaffective Disorder.

**ctiprofile**

38. A Phase 2, Open-Label, Dose Titration Study to Evaluate the Efficacy and Safety of NBI-98854 for the Treatment of Tardive Dyskinesia in Subjects With Schizophrenia or Schizoaffective Disorder.

**ctiprofile**

39. Neurocrine Biosciences Announces That VMAT2 Program Will Move Into Phase II Clinical Trials.

**Media Release**

40. Neurocrine Biosciences Announces Successful Phase IIa Clinical Trial for VMAT2 Inhibitor.

**Media Release**

41. A phase I study of Valbenazine for the treatment of drug-induced dyskinesia

**ctiprofile**

42. Neurocrine Biosciences Announces Notice of Allowance for Composition of Matter Patent on VMAT2 Inhibitor.

**Media Release**

43. Neurocrine Biosciences Announces The FDA Has Granted Fast Track Designation For VMAT2 Inhibitor NBI-98854.

**Media Release**

44. Neurocrine Biosciences Receives Breakthrough Therapy Designation for NBI-98854 in Tardive Dyskinesia.

**Media Release**

45. Neurocrine Biosciences Reports First Quarter 2017 Results.

**Media Release**

46. Neurocrine Announces Initiation of a Long-Term Phase II Clinical Study of VMAT2 Inhibitor Valbenazine in Tourette Syndrome.

**Media Release**

47. A long-term phase II clinical study of valbenazine for the treatment of Tourette Syndrome.

**ctiprofile**

48. Neurocrine Biosciences Reports Third Quarter 2016 Results.

**Media Release**

49. Neurocrine Biosciences Reports Year-End 2015 Results and Provides Investor Update for 2016.

**Media Release**

50. Neurocrine Announces Initiation of Phase II Clinical Study of VMAT2 Inhibitor Valbenazine in Children and Adolescents with Tourette Syndrome.

**Media Release**

51. A Randomized, Double-Blind, Placebo-Controlled Study to Assess the Safety and Efficacy of NBI-98854 in Pediatric Subjects With Tourette Syndrome

**ctiprofile**

52. Neurocrine Announces Completion of Phase II Clinical Study of VMAT2 Inhibitor INGREZZA(Tm) (valbenazine) in Adults with Tourette Syndrome.

**Media Release**

53. Neurocrine Announces Initiation of Phase II Clinical Study of VMAT2 Inhibitor NBI-98854 in Adults with Tourette Syndrome.

**Media Release**

54. A Randomized, Double-Blind, Placebo-Controlled Study to Assess the Safety and Efficacy of NBI-98854 in Adult Subjects With Tourette Syndrome

**ctiprofile**

55. Neurocrine Announces Successful Completion of Phase Ib T-Force Study of VMAT2 Inhibitor NBI-98854 in Adolescents and Children with Tourette Syndrome.

**Media Release**

56. Neurocrine Announces Expansion Of VMAT2 Inhibitor Program With Initiation Of Tourette Syndrome Clinical Study.

**Media Release**

57. A Phase 1b, Open-Label, Multiple-Dose Study to Evaluate the Safety, Tolerability, Pharmacokinetics, and Pharmacodynamics of NBI-98854 in Children and Adolescents With Tourette Syndrome

**ctiprofile**

58. Neurocrine Biosciences Reports Fourth Quarter And Year End 2012 Results.

**Media Release**

59. A phase I study of Valbenazine for the treatment of Huntington's disease

**ctiprofile**

60. A Phase 1, Open-Label Study to Assess the Effect of Ketoconazole on the Pharmacokinetics of NBI-98854 in Healthy Subjects

**ctiprofile**

61. Neurocrine Biosciences Reports First Quarter 2010 Results.

**Media Release**

62. Neurocrine Biosciences Announces the Initiation of Second VMAT2 Phase I Clinical Trial.

**Media Release**

63. Neurocrine Advances VMAT2 Inhibitor Program.

**Media Release**

64. Neurocrine Biosciences Reports Third Quarter 2009 Results.

**Media Release**

65. A Phase 1 Study to Evaluate the Safety, Tolerability, and Pharmacokinetics of a Single Dose of NBI-98854 in Subjects With Mild, Moderate, or Severe Hepatic Insufficiency

**ctiprofile**

66. Neurocrine Biosciences Announces Additional European And United States Patents Issued On Proprietary VMAT2 Inhibitor.

**Media Release**

67. Remington G, Factor S, Comella C, Liang G, Burke J, O'Brien C. Safety and Tolerability of Valbenazine (NBI-98854) in Subjects with Tardive Dyskinesia: Results of Long-Term Exposure Data from Three Studies. AAN-2017 2017; abstr. 2615.

Available from: URL: <http://submissions.mirasmart.com/AAN2017/itinerary/login.asp>

68. Neurocrine Announces American Journal of Psychiatry Publication of Positive Results from Kinect 3 Phase III Study of INGREZZA TM (valbenazine) for the Treatment of Tardive Dyskinesia.

**Media Release**

69. Factor S, Hauser R, Mandri DF, Castro-Gayol J, Jimenez R, Siegert S, et al. A Phase 2 Study of Valbenazine (NBI-98854) for Treatment of Tardive Dyskinesia: KINECT 2. AAN-2016 2016; abstr. S27.007.

Available from: URL: <http://link.adisinsight.com/Dc65G>